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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,552	04/09/2004	Stanislav I. Svctlov	61641(49163)	1304

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EXAMINER

WANG, CHANG YU

ART UNIT	PAPER NUMBER
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1649

MAIL DATE	DELIVERY MODE
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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/821,552

Applicant(s)

SVETLOV ET AL.

Examiner

Chang-Yu Wang

Art Unit

1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,5-15 and 18 is/are pending in the application.
- 4a) Of the above claim(s) 12-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,5-11,15 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) 1,3,5-15 and 18 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION
RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed May 21, 2007 is acknowledged. Claims 2, 4, 16 and 17 are cancelled. Claims 1, 3, 5-15 and 18 are pending in this application. Claims 12-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.
2. Claims 1, 3, 5-11, 15 and 18 are under examination in this office action.
3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.
4. Applicant's arguments filed on May 21, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

5. The rejection of claims 1-11, 15-18 under 35 U.S.C. 112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is withdrawn in response to Applicant's cancellation of claims 2, 4, 16 and 17, and Applicant's amendment by limiting the culture medium and neural cells.

The rejection of claims 1-3, 15, 17, 18 under 35 U.S.C. 102 (b) for being anticipated by US Patent No. 6150345 (issued Nov 21, 2000, priority Aug 18, 1998) is withdrawn in response to Applicant's cancellation of claims 2, 4, 16 and 17 and Applicant's amendment by limiting the culture medium and cells.

The rejection of claims 1-11, 15-18 under 35 U.S.C. 102 (e) for being anticipated by US2004/0014662 (published Jan 22, 2004, priority date Jul 2, 2002) is withdrawn in response to Applicant's cancellation of claims 2, 4, 16 and 17 and Applicant's amendment by limiting the culture medium and cells.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, 5-11, 15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindquist et al. (US2004/0014662, published Jan 22, 2004, priority date Jul 2, 2002 as cited in Paper No. 20061113) in view of Steindler et al. (US 6638763, issued on Oct 23, 2003, priority Jan 7, 1997).

The amended claims are directed to a product comprising neural stem/progenitor cells, LPA and a basal medium comprising insulin, methyl cellulose and free of either EGF or FGF2.

Lindquist et al. (US2004/0014662) teaches a tissue culture system comprising at least one isolated neural stem cell expressing at least one LPA receptor, a LPA compound and a basal culture medium (i.e. as it relates to claim 1; see p. 22, Example 3). Lindquist (US'662) teaches culturing neural stem cells as neurospheres derived from anterior lateral wall of the lateral ventricles of adult mice (i.e. as it relates to claims 5-7) in a neurosphere culture medium, which contains DMEM/F12, B27 supplement, HEPES and 20ng/ml EGF in the presence of LPA, which is therefore free of FGF2 (i.e. as it relates to claims 1, 15; see p. 22, [0218], [0223],[0224]). Lindquist (US'662) teaches isolating neural stem/progenitor cells from the hippocampus and from the ventricular wall as well as tissue adjacent to the ventricular wall, which encompass subependymal zone (i.e. as it relates to claims 1, 5-7, 15 and 18; see p. 3, [0031]). Lindquist (US'662) teaches isolation of cells from mammals including human such as from fetal brain, which is postmortem by definition (i.e. as it relates to claim 8; see p.3, [0034], [0040]). Lindquist (US'662) teaches that LPA at a low concentration (1-10 nM) can enhance proliferation of neural stem/progenitor cells (see p. 23, [0231]) and induce the expression levels of heparin-binding EGF-like growth factors (see p.7, [0086]-[0087]). LPA (LPA 18:1 (oleoyl) disclosed in the Lindquist (US'662) is from the Avanti Polar Lipids Inc., which is the same as in the instant application (i.e. as it relates to claims 1,

Art Unit: 1649

3, 15 and 18; see p. 23, [0223]). However, Lindquist (US'662) does not teach a culture medium for neural stem/progenitor cells containing insulin.

The expression of LPA receptors (LPA1-3 receptors) as recited in claims 1, 9, and 10 is an intrinsic feature of the neural stem cells as evidenced by Hecht et al. (J. Cell Biol. 1996. 135: 1071-1083 as cited in Paper No. 20061113). Hecht et al. teach that neuroblasts derived from developing cerebral cortex expressing LPA1 receptor (also named vzg-1). The expression of Sca-1/AC133 and β III-tubulin and nestin as recited in claims 10 and 11 is also an intrinsic feature of neural stem/progenitor cells as evidenced by Locatelli et al. (J. Hematotherapy & Stem cell Res. 2003. 12: 727-734 as cited in Paper No. 20061113) and Hao et al. (J. Hematotherapy & Stem Cell Res. 2003. 12: 23-32 as cited in Paper No. 20061113). Locatelli et al. teach that neural stem/progenitor cells derived from bone marrow cultured in culture medium for neurospheres express β -III tubulin and nestin and Sca-1 (see p. 727, abstract), while Hao et al. teaches that CD34+/CD133+ (AC133)/CD3- hematopoietic stem cells can differentiate into neural cells (see p. 23, abstract).

In addition, although Lindquist (US'662) does not explicitly teach a basal medium containing methyl cellulose, a basal medium containing methyl cellulose for neural stem/progenitor cells is a commercial culture medium of Stem Cell Technologies, NeuroCult, (p. 8 of the instant specification and the 2003 catalog of Stem Cell Technologies, #03237).

Steindler et al. (US 6638763) teach a culture medium for neural stem/progenitor cells within neurospheres containing methyl cellulose and insulin (i.e. as it relates to

Art Unit: 1649

claim 1; see col. 10-13). However, Steindler et al. do not teach use of LPA in their culture medium.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use a culture medium containing methyl cellulose and insulin for neural stem/progenitor cells. The person of ordinary skill in the art would have been motivated to do so because use of a culture medium containing methyl cellulose and insulin for culturing neural stem/progenitor cells is routine in the art, as exemplified by Steindler et al., and LPA has been shown to induce proliferation of neural stem/progenitor cells as taught by Lindquist (US'662). Thus, one of ordinary skill in the art would have expected success in maintaining and culturing neural stem/progenitor cells in a culture medium containing LPA, insulin, methyl cellulose and free of FGF2.

Conclusion

NO CLAIM IS ALLOWED.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

Art Unit: 1649

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
July 12, 2007


ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER